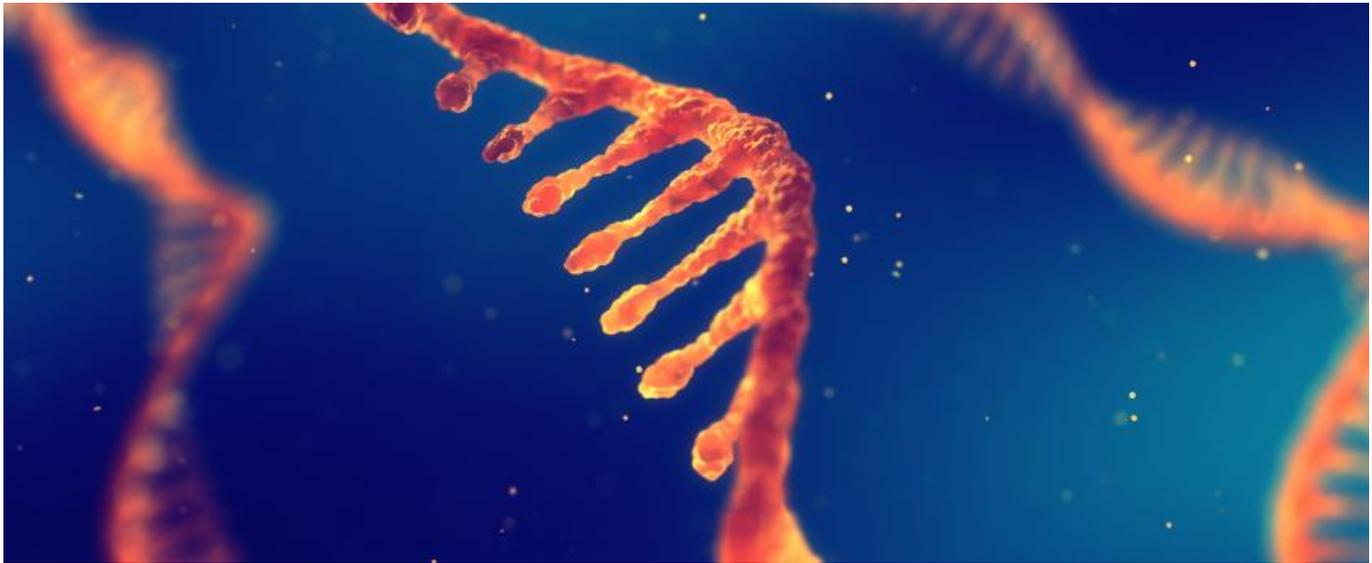


Astrazeneca throws Silence an \$80m lifeline



[Elizabeth Cairns](#)



Silence has received an important validation, but making progress could be tough.

The \$80m cash-and-equity deal Silence Therapeutics signed with AstraZeneca today is an important endorsement of the group's small interfering RNA technology, and has pushed Silence's stock up 23%. Added to Astra's long-running collaboration with Moderna it is plain that the UK giant sees a future in RNA-based technologies.

But the deal calls for delivering siRNA molecules to tissues other than the liver – a tough prospect. Another question is why Astra has roped in Silence rather than the more established RNA interference player Alnylam, particularly since both smaller companies are working on the same means of delivering the nucleic acids – an aspect crucial to the success of these projects.

The \$4bn dream

Today's deal will see Astra and Silence collaborate on developing therapies for cardiovascular, renal, metabolic and respiratory disorders with the initial phase intended to yield five targets within three years. Astra, which has forked over \$60m in cash and a \$20m equity investment, has the option to extend this to a further five targets.

Delivery of siRNA to the liver is an established approach, and Silence achieves this by conjugating the molecules to Galnac, which binds to a receptor on hepatocytes. Pulling off a similar trick in the heart, lungs and kidneys will likely require a different delivery tech; Silence's work with lipid nanoparticles could have application here.

The colossal milestones Silence stands to gain under the deal's terms reflect the difficulties of this kind of development. For each disease target, Silence could be in line for up to \$400m in milestones, plus tiered royalties, giving a potential total value in excess of \$4bn. The actual cash the company comes in for will be a fraction of this, and Silence does not expect its first \$10m fee for the identification of the first molecule to go into testing before 2022.

A shift in priorities

In the interim the up-front cash will sustain Silence beyond 2022, management said on a conference call, and enable it to develop its in-house candidates. It has rejigged its pipeline to prioritise SLN360, an siRNA against apolipoprotein A for the treatment of cardiovascular disease that could yield topline human data around the middle of 2021, the company says.

Its previous lead, the beta-thalassaemia and myelodysplastic syndrome project SLN124, is in [a phase I trial](#) in which dosing had been expected to conclude by the end of this month. The Covid-19 pandemic has put paid to that, the group said, and recruitment is paused. Silence now intends to develop a new protocol with a broader population; the first data could now come in a year or so.

Why Silence, though? Alnylam is a bigger group with proven tech: its Onpattro, a lipid nanoparticle-delivered transthyretin siRNA, was launched in 2018 as a treatment for hereditary amyloidosis. If Astra was looking to add siRNA capabilities to the mRNA-based tech it has thanks to its tie-up with Moderna, Alnylam would have been the logical place to start. Perhaps Alnylam was not interested in the Astra deal, or wanted significantly more than \$80m up front.

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